

CLAIMS

1. A method for modulating metabolism of nitric oxides by varying NO oxidation rate in a heterogeneous medium by changing makeup thereof **characterized in that** the number of phases in this medium and/or one or more volume ratios of phases and/or one or more NO or oxygen distribution coefficients between phases are modified.
2. The method according to claim 1 characterized in that for accelerating NO oxidation with oxygen the changes are carried out in such a way that the values of the expression

$$H = \frac{\sum_{i=1}^{i=n-1} k_i Q_{NO,i}^2 Q_{O_2,i} X_i + k_n \left(1 - \sum_{i=1}^{i=n-1} X_i \right)}{\left(1 + \sum_{i=1}^{i=n-1} Q_{NO,i} X_i - \sum_{i=1}^{i=n-1} X_i \right)^2 \left(1 + \sum_{i=1}^{i=n-1} Q_{O_2,i} X_i - \sum_{i=1}^{i=n-1} X_i \right)}$$

where H is acceleration of NO oxidation reaction with oxygen in heterogeneous n -phasic system as compared to the least hydrophobic (aqueous) phase, k_i is reaction rate constant in i phase, $Q_{NO,i}$, $Q_{O_2,i}$ is a equilibrated distribution coefficient of NO and O_2 in i phase, x_i is a portion of i phase in a total volume, would increase and for slowing down NO oxidation with oxygen the changes are carried out in such a way that the H value would decrease.

3. The method according to any one of claims 1 and 2 **characterized in that** for changing NO distribution coefficients between the phases the medium quantitative makeup is changed

without changing qualitative makeup and/or without forming novel phases.

4. The method according to any one of claims 1 to 3 **characterized in that** one or more components are introduced into heterogeneous medium so that one or more novel phases appear therein.

5. The method according to any one of claims 1 to 4 **characterized in that** the components being introduced comprise one or more compounds selected from the group consisting of: a perfluorohydrocarbone, a halo-substituted perfluorocarbohydra-te derivative and a tertiary perfluoroalkylamine, SF_6 .

6. The method according to any one of claims 1 to 5 **characterized in that** the components being introduced comprise solution of a protein that solubilizes the fluorinated organic compound having the value of distribution coefficients Q_{NO} and/or Q_{O_2} in a biphasic system with water higher than the maximum value of Q_{NO} and/or Q_{O_2} for arbitrary pair of phases of reaction mixture before introducing.

7. The method according to any one of claims 1 to 6 **characterized in that** the heterogeneous medium is blood plasma.

8. The method according to any one of claims 1 to 6 **characterized in that** the heterogeneous medium is blood.

9. The method according to any one of claims 1 to 8 **characterized in that** the components comprising one or more catalysts and/or renitrosation inhibitors are additionally introduced.

10. The method according to any one of claims 1 to 9 **characterized in that** the components comprising one or more reducers are additionally introduced.

11. The method according to any one of claims 1 to 10 **characterized in that** the components comprising one or more scavengers of free radicals are additionally introduced.

12. The method according to any one of claims 1 to 11 **characterized in that** the components comprising one or more compounds producing a nitrosocompound and/or releasing nitrogen as affected by NO oxidation products are additionally introduced.

13. The method according to any one of claims 1 to 12 **characterized in that** additionally the temperature of the heterogeneous medium or of a portion thereof is modified.

14. Compositions comprising a perfluororganic compound resistant in metabolic reactions and forming with water a heterogeneous mixture said compound being selected from the group including: perfluorohydrocarbons, halo-derivatives of perfluorohydrocarbons, 0.1 to 90% perfluoroalkylamines and one or more compounds of the group: SF₆, perfluorohydrocarbons, halo-derivatives of perfluorohydrocarbons, tertiary perfluoroalkylamines, water up to 100% for modulating metabolism of nitric oxides.

15. The composition according to claim 14 **characterized in that** one or more compounds belonging to one or more groups from the following list are additionally introduced therein: emulsifiers, biologically compatible salts for maintaining pH and/or ionic

strength, carbohydrates for maintaining osmotic pressure and/or one or more compounds belonging to one or more groups of the following list: catalysts or inhibitors of pernitrosification, reducers, scavengers of free radicals, targets for nitrosation and/or precursors thereof, targets for nitrosation with nitrogen release.

16. The composition according to claim 15 **characterized in that** copolymers of ethylene oxide and of propylene oxide and/or phospholipids are introduced as emulsifiers.

17. The compositions according to any one of claims 15 and 16 **characterized in that** they are emulsions of the fluorine comprising compounds with average size of micellae less than 100 nm.

18. The compositions according to any one of claims 15 to 17 **characterized in that** glucose and/or fructose and/or saccharose are introduced as carbohydrates for maintaining osmotic pressure.

19. The compositions according to any one of claims 15 to 18 **characterized in that** ascorbic acid and/or salts thereof and/or retinol and/or acyclic derivatives thereof are introduced as reducers.

20. The compositions according to any one of claims 15 to 19 **characterized in that** one or more substituted or unsubstituted mono- and/or di- and/or polyphosphates and/or complexes thereof with magnesium or zinc or copper or manganese are introduced as catalysts or renitrosation inhibitors.

21. The compositions according to any one of claims 15 to 20 **characterized in that** one or more compounds of the group: thiourea, thioamides, methionine, arginine, peptides and/or acyclic and/or amide derivatives thereof of general formula X-Pept-Y, where X=H or acyl, Y=OH or -NH₂ or NHR or NR₁R₂, Pept=peptide comprising residues of methionine and/or aspartic acid and/or histidine and/or glutamic acid and/or arginine, are introduced as catalysts or renitrosation inhibitors.
22. The composition according to claim 21, **characterized in that** Pept comprises a fragment Met-Glu-His-Phe.
23. The composition according to any one of claims 21 or 22, **characterized in that** Pept is Met-Glu-His-Phe-Pro-Gly-Pro and all the amino acids belong to L-series.
24. The composition according to any one of claims 15-23 **characterized in that** tocopherol and/or acyclic derivatives thereof are introduced as scavengers of free radicals.
25. The composition according to any one of claims 15-24 **characterized in that** one or more thiols or dithiols or disulphides are introduced as targets for nitrosation and/or precursors thereof.
26. The composition according to any one of claims 15-25 **characterized in that** one or more compounds from the group: dithiopropanol, dithiobutanediol, lipoic acid, dihydrolipoic acid, cysteine, homocysteine, peptides comprising cysteine and/or cystine, acyclic and/or esteric and/or amide derivatives of cysteine or cystine or peptides comprising these amino acids

or protein, are introduced as targets for nitrosation and/or precursors thereof.

27. The compositions according to any one of claims 15-26 **characterized in that** one or more compounds from the group: urea, sulfaminic acid and salts thereof, amidophosphoric acid and salts thereof, carbamic acid and salts thereof, asparagine, aspartic acid and salts thereof, glutamine and salts thereof, glutaminic acid and salts thereof, peptides comprising asparagine and/or glutamine, primary amine or salts thereof are introduced as targets for nitrosation with nitrogen release.

28. The compositions according to any one of claims 15-26 **characterized in that** they are emulsions that have distribution dependencies of the number of particle by size with more than one maximum and/or they are compositions prepared by mixing two or more compositions according to claims 14-27.

29. A use of blood substitutes based on stabilized emulsions of the fluorine comprising compounds for modifying NO oxidation rate.

30. A method for effecting organism of a patient in need of correcting metabolism of nitric oxides **characterized in that** for modifying NO oxidation rates and subsequent reaction the number of phases is modified in the organism and environment thereof and/or one or more ratios between volumes of the phases and/or one or more distribution coefficients of NO or oxygen between the phases.

31. The method according to claim 30 **characterized in that** a patient is orally administered a composition comprising one or

more water immiscible fluorine comprising compounds and resistant in metabolism reactions and/or this composition is used locally for contacting a skin tegument site or a wound.

32. The method according to claim 31 **characterized in that** one or more compounds from the group: water, emulsifier, biologically compatible salts maintaining pH and/or ionic strength, carbohydrates for maintaining osmotic pressure and/or one or more compounds belonging to one or more groups of the following list: catalysts or inhibitors of pernitrosification, reducers, scavengers of free radicals, targets for nitrosation and/or precursors thereof, targets for nitrosation with nitrogen release.

33. The method according to any one of claims 31 and 32 **characterized in that**

one or more compounds from the group: a perfluorohydrocarbon, a perfluorohydrocarbon halo-substituted derivative and a tertiary perfluoroalkylamine are introduced as the fluorine comprising water immiscible compounds;

copolymers of ethylene oxide and of propylene oxide and/or phospholipids are introduced as emulsifiers;

and/or glucose and/or fructose and/or saccharose are introduced as carbohydrates for maintaining osmotic pressure;

and/or ascorbic acid and/or salts thereof and/or retinol and/or acyclic derivatives thereof are introduced as reducers;

and/or one or more substituted or unsubstituted mono- and/or di- and/or polyphosphates and/or complexes thereof with magnesium or

zinc or copper or manganese are introduced as catalysts or renitrosation inhibitors;

and/or thiourea, thioamides, methionine, arginine, peptides and/or acyclic and/or amide derivatives thereof of general formula X-Pept-Y, where X=H or acyl, Y=OH or -NH₂ or NHR or NR₁R₂, Pept=peptide comprising residues of methionine and/or aspartic acid and/or histidine and/or glutamic acid and/or arginine, and/or Pept comprises a fragment Met-Glu-His-Phe; and/or Pept = Met-Glu-His-Phe-Pro-Gly-Pro are introduced as catalysts or renitrosation inhibitors;

and/or tocopherol and/or acyclic derivatives thereof are introduced as scavengers of free radicals;

and/or one or more thiols or dithiols or disulphides and/or one or more compounds from the group: dithiopropanol, dithiobutanol, lipoic acid, dihydrolipoic acid, cysteine, homocysteine, peptides comprising cysteine or cystine, acyclic and/or esteric and/or amide derivatives of cysteine or cystine or peptides comprising these amine acids, or protein are introduced as the targets for nitrosation and/or precursors thereof;

and/or one or more compounds from the group: urea, glutamic, aspartic, carbamic, amidophosphoric, sulfamic acids and salts thereof, asparagine, glutamine, primary amine and salts thereof, peptides comprising asparagine and/or glutamine are introduced as the targets for nitrosation with nitrogen release.

34. The method according to any one of claims 31-33 **characterized in that** several compositions are used simultaneously or sequentially and/or the compositions are

emulsions that have distribution dependencies of the number of particle by size with more than one maximum and/or they are compositions prepared by mixing two or more compositions ~~(according to any one of claims 30-32.)~~

35. The method according to any one of claims 31-34 **characterized in that** the composition is administered intravenously.

36. The method according to any one of claims 31-35 **characterized in that** the composition is administered by inhalation.

37. The method according to any one of claims 30-36 **characterized in that** a patient is additionally administered catalysts or renitrosation inhibitors.

38. The method according to any one of claims 30-37 **characterized in that** a patient is additionally administered diuretics.

39. The method according to any one of claims 30-38 **characterized in that** a patient is additionally administered inhibitors of NO-synthases.

40. The method according to any one of claims 30-39 **characterized in that** a patient is additionally administered NO donors and/or NO inhalation is performed.

41. The method according to any one of claims 30-40 **characterized in that** a patient or one or more individual organs and/or body parts are additionally subjected to the effect of hypothermia and/or infrared irradiation.

42. The method according to any one of claims 30-41 **characterized in that** a patient or a part of his body surface are under the conditions of increased relative humidity.

43. The method according to any one of claims 30-42 **characterized in that** a patient or one or more individual organs and/or body parts are additionally subjected to the effect of low temperature.

44. The method according to any one of claims 30-43 **characterized in that** a patient and/or a part of body surface and/or an individual organ are additionally subjected to the effect of a gas mixture of oxygen with one or more gases from the group of SF₆, N₂, CO₂, NO at partial pressures thereof different from the usual ones in the air makeup at atmospheric pressure and/or said gas mixture is used for respiration of the patient.

45. The method according to any one of claims 30-44 **characterized in that** the patient belongs to the group at risk of septic shock or under the condition of septic shock.

46. The method according to any one of claims 30-44 **characterized in that** the patient belongs to the group at risk of hypoxia or pulmonary edema.

47. The method according to any one of claims 30-44 **characterized in that** the patient belongs to the group at risk of cancer disease or cancer patients.

48. The method according to any one of claims 30-44 **characterized in that** the patient belongs to the group of patients suffering from bronchial asthma.

49. The method according to any one of claims 30-44 **characterized in that** the patient belongs to the group of patients suffering from infectious diseases.
50. The method according to any one of claims 30-44 **characterized in that** the patient belongs to the group of burned patients.
51. The method according to any one of claims 30-44 **characterized in that** the patient belongs to the group of patients in postoperative period.
52. The method according to any one of claims 30-44 **characterized in that** the patient belongs to the group at risk of stroke or of those who sustained stroke.
53. The method according to any one of claims 30-44 **characterized in that** the patient belongs to the group at risk of infarction or of those who sustained infarction.
54. The method according to any one of claims 30-44 **characterized in that** the patient belongs to the group at risk of atherosclerosis or patients suffering from atherosclerosis.
55. The method according to any one of claims 30-44 **characterized in that** the patient belongs to the group at risk of blood coagulation pathology or to patients suffering from blood coagulation pathology.
56. A use of steam bath or sauna for modulating metabolism of nitric oxides by modifying NO oxidation rate.